IN THE SPECIFICATION:

Please amend paragraph number **[0001]** as follows:

[0001] This application claims the priority of provisional application Serial No. 60/392,004, filed June 26, 2002, which is incorporated herein by reference.

Please amend paragraph number **[0002]** as follows:

[0002] The present invention relates to osmotic systems for delivering beneficial agents. More particularly, the present invention relates to an osmotic pump having a minimally compliant, ~~volume efficient~~ volume-efficient piston.

Please amend paragraph number **[0005]** as follows:

[0005] In some instances, a piston is required to separate the beneficial agent from the osmotic agent to prevent the osmotic agent from mixing with or contaminating the beneficial agent. Examples of systems that use a piston to separate the beneficial agent from the osmotic agent include U.S. Patent Nos. 4,753,651; 4,874,388; 4,969,884; 5,030,216; 5,034,229; 5,137,727; 5,180,591; 5,209,746; 5,221,278; 5,234,424; 5,234,692; 5,308,348; 5,318,558; 5,456,679; 5,540,665; 5,690,952; 5,728,088; 5,728,396; 5,795,591; 5,861,166; 5,871,770; 5,985,305; 5,997,527; 6,132,420; 6,156,331; 6,217,906; 6,261,584; 6,287,295; and 6,395,292; and PCT publication WO 99/33446, the entire disclosures of ~~all of which~~ each are herein incorporated by reference. Where the dimensions of the pistons included in the osmotic pumps ~~described~~ claimed in the cited references are described, the ratio of ~~length to total width~~ length-to-total-width of the piston is typically ~~1.5:1.~~ lengthen 1:0:1. However, the cited references do not provide details regarding the ratio of the core of the pistons to the total diameter of the pistons used in these systems described therein. The structure of the capsules described in the cited references is such that the capsule does not expand significantly when the osmotic agent takes in water and expands. As the osmotic agent included in the systems described in the cited references expands, pressure causes the piston to move and the beneficial

agent to be discharged through the delivery orifice at the same rate as the liquid, which is typically water, enters the osmotic agent by osmosis. The osmotic pumps described in the cited references may be designed to deliver a beneficial agent at a controlled constant rate, a varying rate, or in a pulsatile manner.

Please amend paragraph number **[0010]** as follows:

[0010] In one aspect, the present invention includes an osmotic pump that includes a capsule. The capsule is impermeable to liquids and has an interior for holding a beneficial agent. The interior of the capsule has an interior surface. An osmotic agent is located in the interior of the capsule. A semipermeable body is in liquid communication with the capsule and permits liquid to permeate through the semipermeable body to the osmotic agent. A piston is located within the interior of the liquid impermeable capsule. The piston is movable with respect to the interior surface of the ~~capsule,~~ capsule and defines a movable seal with the interior surface of the capsule. The movable seal defined by the piston separates the osmotic agent from the beneficial agent. The piston has at least one annular ring or rib that forms a seal between the piston and the interior surface of the capsule. The osmotic agent is located between the piston and the semipermeable body. The osmotic agent imbibes liquid from a surrounding environment through the semipermeable body to cause the piston to move and in turn cause delivery of the beneficial agent from the capsule.

Please amend paragraph number **[0012]** as follows:

[0012] In yet another aspect, the present invention includes a capsule and a piston having one or more annular rings or ribs ~~(ring, rings, rib, and ribs~~ ("ring," "rings," "rib," and "ribs" are used interchangeably unless otherwise noted), wherein the one or more annular rings provided on the piston have a shallow profile that works to reduce the space for air entrapment during insertion of the piston into the capsule. Such a ring profile is obtained by the piston having a ratio of ~~core diameter to total width or diameter~~ core-diameter-to-total-width-or-diameter of about 0.9:1.

Where the osmotic pump of the present invention includes a piston having rings or ribs characterized by a shallow profile, the rings or ribs may be designed to reduce the springiness and linear compressibility of the piston.

Please amend paragraph number **[0013]** as follows:

[0013] Other objects, advantages and features associated with the present invention will become readily apparent to those skilled in the art from the following detailed description. As will be realized, the invention is capable of modification in various obvious aspects, all without departing from the invention. Accordingly, the drawings and the description are to be regarded as illustrative in ~~nature,~~ nature and not limitative.

Please amend paragraph number **[0014]** as follows:

[0014] The invention will be described in greater detail with reference to the accompanying drawings in which like elements bear like reference numerals, and wherein:

FIG. 1 is a cross-sectional view of an osmotic pump according to the present ~~invention.~~ invention;

FIG. 2 is a cross-sectional view of a piston according to one embodiment of the present ~~invention.~~ invention; and

FIG. 3 is an end view of a piston according to one embodiment of the present invention.

Please amend paragraph number **[0015]** as follows:

[0015] The present invention provides a device for the delivery of a beneficial agent to a fluid environment of ~~use, said device~~ use that includes a ~~volume efficient~~ volume-efficient piston that minimizes leakage between the beneficial agent and the osmotic agent and enables larger beneficial agent and/or osmotic agent payloads.

Please amend paragraph number **[0016]** as follows:

[0016] The term "beneficial agent" ~~intends the~~ is intended to include beneficial ~~agent(s) optionally~~ agent(s), optionally, in combination with pharmaceutically acceptable carriers and, ~~optionally~~ optionally, additional ingredients such as antioxidants, stabilizing agents, etc.

Please amend paragraph number **[0017]** as follows:

[0017] ~~By the time to "start-up" of delivery~~ Use of the terms "time to start-up of delivery" is intended to mean the time from insertion into the fluid environment of use until the beneficial agent is actually delivered at a rate not less than approximately 70% of the intended steady-state rate.

Please amend paragraph number **[0018]** as follows:

[0018] The term "impermeable" ~~intends~~ means that the material is sufficiently impermeable to environmental ~~fluids~~ fluids, as well as ingredients contained within the dispensing ~~device~~ device, such that the migration of such materials into or out of the device through the impermeable device is so low as to have substantially no adverse impact on the function of the device during the delivery period.

Please amend paragraph number **[0019]** as follows:

[0019] The term "semipermeable" ~~intends~~ means that the material is permeable to external fluids but substantially impermeable to other ingredients contained within the dispensing device and the environment of use.

Please amend paragraph number **[0020]** as follows:

[0020] The beneficial agent delivery devices of the present invention find use where the prolonged and controlled delivery of a beneficial agent is desired. In many ~~cases~~ cases, the

beneficial agent is susceptible to degradation if exposed to the environment of use prior to ~~delivery and the~~ delivery. The delivery devices protect the agent from such exposure.

Please amend paragraph number **[0021]** as follows:

[0021] As shown in FIG. 1, the present invention relates to an osmotic pump 20 for delivering a beneficial agent 24. The osmotic pump 20 includes a minimally compliant, ~~volume efficient~~ volume-efficient piston 30. The osmotic pump 20 also includes ~~an~~ a capsule 22 that encloses the piston 30 and an osmotic agent 26. The piston 30 is movable within the capsule 22 and defines a ~~moveable~~ movable seal that substantially prevents the osmotic agent 26 and the beneficial agent 24 from adversely affecting one another. The piston 30 includes at least one annular ring or ~~rib~~ rib, such that when the piston is inserted into the capsule 22, the ~~said~~ ring or rib forms, along with the core of the ~~piston~~ piston, a fluid seal with the interior surface of the capsule 22. A semipermeable body 28 is in liquid communication with the osmotic agent 26 and permits liquid to permeate through the semipermeable body 28 to the osmotic agent 26. The osmotic agent 26 imbibes the liquid from a surrounding environment and causes the piston 30 to move, which, in turn, causes the beneficial agent 24 to be released from the osmotic pump 20.

Please amend paragraph number **[0022]** as follows:

[0022] The configuration of the osmotic pump ~~20~~ 20, according to the present invention illustrated in FIG. ~~1 is~~ 1, is one example of an osmotic delivery device and is not to be construed as limiting the present invention. The present invention is generally applicable to all osmotic delivery devices having any number of shapes, and to all such devices administered in any variety of methods, such as oral, ruminal, and implantable osmotic delivery techniques.

Please amend paragraph number **[0023]** as follows:

[0023] The capsule 22 of the osmotic pump 20 encloses or contains the osmotic agent 26 and the piston body 32. The capsule 22 includes a tubular or elongated and

substantially cylindrical capsule 22 illustrated in FIG. 1. The capsule 22 has a first opening 51 at a first end 50 and a second opening 53 at a second end 52 opposite the first end 50. The capsule 22 also includes the semipermeable body 28 that obstructs, blocks, ~~closes off,~~ closes off, or plugs the first opening 51 in the capsule 22 to enclose the osmotic agent 26 and piston body 32. Thus, the first opening 51 receives the semipermeable body 28.

Please amend paragraph number **[0024]** as follows:

[0024] The capsule 22 also includes a delivery port 44 located at the second end 52 of the capsule 22. As beneficial agent 24 is delivered from the osmotic pump 20, the beneficial agent is expelled through the delivery port 44. The delivery port 44 may be an orifice formed by conventional techniques. Included among these methods are mechanical drilling, laser drilling, and molding. The capsule 22 will contain at least one such delivery port ~~44, and~~ 44 and, in most configurations, one delivery port 44 will suffice. However, two or more delivery ports 44 may be present without departing from the present invention. The delivery port 44 may be formed in the capsule 22 itself, or may be formed in a separate and distinct plug-like member for insertion into the second opening 53 of the capsule 22. The delivery port 44 can be a slit orifice, such as that disclosed in U.S. Patent No. 5,997,527, the entire disclosure of which is hereby incorporated by reference, or a spiral orifice, such as that disclosed in U.S. Patent No. 5,728,396, the entire disclosure of which is hereby incorporated by reference.

Please amend paragraph number **[0025]** as follows:

[0025] The delivery port 44 is made of an inert and biocompatible material selected ~~from~~ from, but not limited ~~to~~ to, metals ~~including~~ including, but not limited ~~to~~ to, titanium, stainless steel, platinum and their alloys and cobalt-chromium alloys and the like, and polymers ~~including~~ including, but not limited ~~to~~ to, polyethylene, polypropylene, polycarbonate and polymethylmethacrylate and the like.

Please amend paragraph number **[0026]** as follows:

[0026] The dimensions of the delivery port 44 in terms of both diameter and length will vary with the type of beneficial agent 24, the rate at which the beneficial agent is to be delivered, and the environment into which it is to be delivered. The considerations involved in determining the optimum dimensions of the delivery port 44 for any particular capsule or beneficial agent 24 are the same as those for delivery ports or orifices of capsules in the prior art, and selection of the appropriate dimensions will be readily apparent to those skilled in the art.

Please amend paragraph number **[0029]** as follows:

[0029] Materials suitable for construction of the capsule 22 include, but are not limited to, non-reactive polymers or biocompatible metals, alloys, or elastomers. The polymers include acrylonitrile polymers such as acrylonitrile-butadiene-styrene terpolymer, and the like; halogenated polymers such as polytetrafluoroethylene, polychlorotrifluoroethylene, copolymer tetrafluoroethylene and hexafluoropropylene; polyimide; polysulfone; polycarbonate; polyethylene; polypropylene; ~~polyvinylchloride-acrylic~~ polyvinylchloride-acrylic copolymer; polycarbonate-acrylonitrile-butadiene-styrene; ~~polystyrene;~~ polystyrene, and the like. Metallic materials useful for the capsule 22 include stainless steel, titanium, platinum, tantalum, gold, and their alloys, as well as gold-plated ferrous alloys, ~~platinum-plated~~ platinum-plated ferrous alloys, cobalt-chromium alloys and titanium ~~nitride coated~~ nitride-coated stainless steel. Elastomers useful for the capsule 22 include fluorinated or perfluorinated rubbers (e.g., Viton®). The capsule 22 can be formed from any of the above-mentioned wall-forming materials by use of a mold, with the materials applied either over the mold or inside the mold, depending on the mold configuration. Additionally, the capsule 22 can be formed by machining. Any of the wide variety of techniques known in the pharmaceutical industry can be used to form the capsule 22.

Please amend paragraph number **[0031]** as follows:

[0031] The osmotic agent 26 is a liquid-attracting agent used to drive the flow of the beneficial agent 24 from the osmotic pump 20. The osmotic agent 26 may be an osmagent, an osmopolymer, or a mixture of the two. Species that fall within the category of osmagent, i.e., the non-volatile species which are soluble in water and create the osmotic gradient driving the osmotic inflow of water, vary widely. Examples are well known in the art and include magnesium ~~sulfate,~~ sulfate; magnesium ~~chloride,~~ chloride; potassium ~~sulfate,~~ sulfate; sodium ~~chloride,~~ chloride; sodium ~~sulfate,~~ sulfate; lithium ~~sulfate,~~ sulfate; sodium ~~phosphate,~~ phosphate; potassium ~~phosphate, d-mannitol, sorbitol, inositol, urea,~~ phosphate; d-mannitol; sorbitol; inositol; urea; magnesium ~~succinate,~~ succinate; tartaric ~~acid, raffinose,~~ acid; raffinose and various ~~monosaccharides,~~ monosaccharides; oligosaccharides and ~~polysaccharides~~ polysaccharides, such as sucrose, glucose, lactose, fructose, and ~~dextran,~~ dextran; as well as mixtures of any of these various species.

Please amend paragraph number **[0032]** as follows:

[0032] Species that fall within the category of osmopolymer are hydrophilic polymers that swell upon contact with water, and these vary widely as well. Osmopolymers may be of plant or animal origin, or synthetic, and examples of osmopolymers are well known in the art. Examples include: poly(hydroxy-alkyl methacrylates) with molecular weight of 30,000 to 5,000,000; poly(vinylpyrrolidone) with molecular weight of 10,000 to 360,000; anionic and cationic hydrogels; polyelectrolyte complexes; poly(vinyl alcohol) having low acetate residual, optionally cross-linked with glyoxal, formaldehyde or glutaraldehyde and having a degree of polymerization of 200 to 30,000; a mixture of methyl cellulose, cross-linked agar and carboxymethylcellulose; a mixture of hydroxypropylmethylcellulose and sodium carboxymethylcellulose; polymers of N-vinyllactams; ~~polyoxyethylene-polyoxypropylene~~ polyoxyethylene-polyoxypropylene gels; polyoxybutylene-polyethylene block copolymer gels; carob gum; polyacrylic gels; polyester gels; polyurea gels; polyether gels; polyamide gels;

polypeptide gels; polyamino acid gels; polycellulosic gels; carbopol acidic carboxy polymers having molecular weights of 250,000 to 4,000,000; Cyanamer polyacrylamides; cross-linked indene-maleic anhydride polymers; Good-Rite polyacrylic acids having molecular weights of 80,000 to 200,000; Polyox Polyethylene oxide polymers having molecular weights of 100,000 to 5,000,000; starch graft copolymers; and Aqua-Keeps acrylate polymer polysaccharides.

Please amend paragraph number **[0033]** as follows:

[0033] The osmotic agent 26 may be manufactured by a variety of techniques, many of which are known in the art. In one such technique, an osmotically active agent is prepared as solid or semi-solid formulations and pressed into pellets or tablets whose dimensions correspond to slightly less than the internal dimensions of the respective chambers that they will occupy in the capsule interior. Depending on the nature of the materials used, the agent and other solid ingredients that may be ~~included,~~ included can be processed prior to the formation of the pellets by such procedures as ballmilling, calendaring, stirring or rollmilling to achieve a fine particle size and hence fairly uniform mixtures of each.

Please amend paragraph number **[0035]** as follows:

[0035] Patients to whom beneficial agents 24 may be administered using systems of this invention include humans and animals. The invention is of particular interest for application to humans and household, sport, and farm animals, particularly mammals. For the administration of beneficial agents, the devices of the present invention may be implanted subcutaneously or ~~intraperitoneally~~ intraperitoneally, wherein aqueous body fluids or liquids are available to activate the osmotic agent 26. Devices of the invention may also be administered to the rumen of ruminant animals, in which embodiment the devices may further comprise a conventional density element for maintaining the device in the rumen for extended periods of time of up to 120 days or longer.

Please amend paragraph number **[0037]** as follows:

[0037] Drug agents that may be delivered by the present invention include drugs which act on the peripheral nerves, adrenergic receptors, cholinergic receptors, the skeletal muscles, the cardiovascular system, smooth muscles, the blood circulatory system, synoptic sites, neuroeffector junctional sites, endocrine and hormone systems, the immunological system, the reproductive system, the skeletal system, autoacoid systems, the alimentary and excretory systems, the histamine system and the central nervous system. Suitable agents may be selected from, for ~~example~~ example, proteins, enzymes, hormones, polynucleotides, nucleoproteins, polysaccharides, glycoproteins, lipoproteins, polypeptides, steroids, analgesics, local anesthetics, antibiotic agents, anti-inflammatory corticosteroids, ocular drugs and synthetic analogs of these species.

Please amend paragraph number **[0038]** as follows:

[0038] Examples of drugs that may be delivered by devices according to this invention include, but are not limited to, prochlorperzine edisylate, ferrous sulfate, aminocaproic acid, mecamylamine hydrochloride, procainamide hydrochloride, amphetamine sulfate, methamphetamine hydrochloride, benzamphetamine hydrochloride, isoproterenol sulfate, phenmetrazine hydrochloride, bethanechol chloride, methacholine chloride, pilocarpine hydrochloride, atropine sulfate, scopolamine bromide, isopropamide iodide, tridihexethyl chloride, phenformin hydrochloride, methylphenidate hydrochloride, theophylline cholinate, cephalexin hydrochloride, diphenidol, meclizine hydrochloride, prochlorperazine maleate, phenoxybenzamine, thiethylperzine maleate, anisindone, diphenadione erythrityl tetranitrate, digoxin, isofluorphate, acetazolamide, methazolamide, bendroflumethiazide, chloropromaide, tolazamide, chlormadinone acetate, phenaglycodol, allopurinol, aluminum aspirin, methotrexate, acetyl sulfisoxazole, ~~erthromycin,~~ erythromycin, hydrocortisone, hydrocorticosterone acetate, cortisone acetate, dexamethasone and its derivatives such as betamethasone, triamcinolone, methyltestosterone, 17-β-Estradiol, ethinyl estradiol, ethinyl estradiol 3-methyl ether,

prednisolone, 17-α-hydroxyprogesterone acetate, 19-nor-progesterone, norgestrel, norethindrone, norethisterone, norethiederone, progesterone, norgesterone, norethynodrel, aspirin, indomethacin, naproxen, fenoprofen, sulindac, indoprofen, nitroglycerin, isosorbide dinitrate, propranolol, timolol, atenolol, alprenolol, cimetidine, clonidine, imipramine, levodopa, chlorpromazine, methyldopa, dihydroxyphenylalanine, theophylline, calcium gluconate, ketoprofen, ibuprofen, cephalexin, ~~erthromycin, haloperidol.~~ erythromycin, haloperidol, zomepirac, ferrous lactate, vincamine, diazepam, phenoxybenzamine, diltiazem, milrinone, capropril, mandol, quanbenz, hydrochlorothiazide, ranitidine, flubiprofen, fenufen, fluprofen, tolmetin, alcofenac, mefenamic, flufenamic, difiuinal, nimodipine, nitrendipine, nisoldipine, nicardipine, felodipine, lidoflazine, tiapamil, gallopamil, amlodipine, mioflazine, lisinolpril, enalapril, enalaprilat, captopril, ramipril, famotidine, nizatidine, sucralfate, etintidine, tetratolol, minoxidil, chlordiazepoxide, diazepam, amitriptyline, and imipramine. Further examples are proteins and peptides which include, but are not limited to, insulin, colchicine, glucagon, ~~thyroid stimulating~~ thyroid-stimulating hormone, parathyroid and pituitary hormones, calcitonin, rennin, prolactin, corticotrophin, thyrotropic hormone, ~~follicle stimulating~~ follicle-stimulating hormone, chorionic gonadotropin, ~~gonadotropin releasing~~ gonadotropin-releasing hormone, bovine somatotropin, porcine somatotropin, oxytocin, vasopressin, GRF, somatostatin, lypressin, pancreozymin, luteinizing hormone, LHRH, LHRH agonists and antagonists, leuprolide, interferons (including alpha, beta, delta, and gamma), interleukins, growth hormones such as human growth hormone, bovine growth hormone and porcine growth hormone, fertility inhibitors such as the ~~protaglandins,~~ prostaglandins, fertility promoters, growth factors, coagulation factors, human pancreas ~~hormone releasing~~ hormone-releasing factor, analogs and derivatives of these compounds, and pharmaceutically acceptable salts of these compounds, or their analogs or derivatives.

Please amend paragraph number **[0040]** as follows:

[0040] Osmotic pumps according to the present invention are also useful in environments outside of physiological or aqueous environments. For example, the osmotic pump may be used in intravenous systems (attached to an IV pump or bag or to an IV bottle, for

example) for delivering beneficial agents to an animal or human. Osmotic ~~pumps~~ pumps, according to the present ~~invention~~ invention, may also be utilized in blood oxygenators, kidney dialysis and electrophoresis, for example.

Please amend paragraph number **[0041]** as follows:

[0041] The osmotic pump 20 also includes the aforementioned semipermeable body 28, such as the semipermeable plug illustrated in FIG. 1. The semipermeable body 28 is formed of a semipermeable material that allows liquid to pass from an exterior environment of use into the capsule 22 to cause the osmotic agent 26 to swell. ~~But~~ However, the material forming the semipermeable body 28 is largely impermeable to the materials within the capsule and other ingredients within the environment of use. As illustrated in FIG. 1, the semipermeable body 28 is in the shape of a plug that is inserted into the first opening 51 of the capsule 22 at the first end 50, closing off the first opening 51 of the capsule 22. The semipermeable body 28 may also be a membrane coating on the exterior surface of the capsule 22 or a sleeve or cap that slides over a portion of the capsule 22 to enclose the osmotic agent 26.

Please amend paragraph number **[0042]** as follows:

[0042] As shown in FIG. 1, the osmotic pump 20 includes the semipermable body 28, such as the semipermeable plug illustrated. The semipermeable body 28 is typically cylindrically ~~shaped,~~ shaped and has means for sealing or ribs 46 extending outwardly from the outer surface of the semipermeable body 28. The ribs 46 are the means by which the semipermeable ~~plug~~ body 28 operates like a cork or stopper, obstructing and plugging ~~the~~ first opening 51 in the capsule 22 of the osmotic pump 20 as illustrated in FIG. 1. The means for sealing ~~46 may~~ may be the exemplary ribs 46, or may be other configurations such as threads, a tight interference fit between an outer sealing surface of the plug and the capsule 22, glue, adhesives, ridges, lips, or other devices which join the semipermeable body 28 with the capsule 22 to prevent leakage. The semipermeable body 28 is, therefore, intended for at least partial insertion into an opening of the

capsule 22, and the means for ~~sealing 46~~ sealing keeps the environment of use from ~~an~~ the inside of the capsule 22 and prevents liquid and other substances in the environment of use, besides the permeation liquid, from entering the osmotic pump ~~20~~ 20, while also preventing materials from the inside of the delivery system from leaking or escaping to the environment of use.

Please amend paragraph number **[0044]** as follows:

[0044] Semipermeable compositions suitable for the semipermeable body 28 are well known in the art, examples of which are disclosed in U.S. Patent No. 4,874,388, the entire disclosure of which is incorporated herein by reference. Such possible semipermeable materials from which the body 28 can be made include, but are not limited to, for example, ~~Hytrel~~ Hytrel® polyester elastomers (DuPont), cellulose esters, cellulose ethers and cellulose ester-ethers, water ~~flux enhanced~~ flux-enhanced ethylene-vinyl acetate copolymers, semipermeable membranes made by blending a rigid polymer with water-soluble low molecular weight compounds, and other semipermeable materials well known in the art. The above cellulosic polymers have a degree of ~~substitution, D.S.,~~ substitution ("D.S.") on the ~~anydroglucose~~ anhydroglucose unit, from greater than 0 up to 3 inclusive. By, "degree of ~~substitution," or "D.S.,"~~ substitution" or "D.S." is meant the average number of hydroxyl groups originally present on the anhydroglucose unit comprising the cellulose polymer that are replaced by a substituting group. Representative materials include, but are not limited to, one selected from the group consisting of cellulose acylate, cellulose diacetate, cellulose triacetate, mono-, di-, and tricellulose alkanylates, mono-, di-, and tricellulose aroylates, and the like. Exemplary cellulosic polymers include cellulose acetate having a D.S. up to 1 and an acetyl content up to 21%; cellulose acetate having a D.S. of 1 to 2 and an acetyl content of 21% to 35%; cellulose acetate having a D.S. of 2 to 3 and an acetyl content of 35% to 44.8%, and the like. More specific cellulosic polymers include cellulose propionate having a D.S. of 1.8 and a propionyl content of 39.2% to 45% and a hydroxyl content of 2.8% to 5.4%; cellulose acetate butyrate having a D.S. of 1.8 and an acetyl content of 13% to 15% and a butyryl content of 34% to 39%; cellulose acetate butyrate having an acetyl content of

2% to 29%, a butyryl content of 17% to 53% and a hydroxyl content of 0.5% to 4.7%; cellulose acetate butyrate having a D.S. of 1.8, and an acetate content of 4% average weight percent and a butyryl content of 51%; cellulose triacylates having a D.S. of 2.9 to 3 such as cellulose trivalerate, cellulose trilaurate, cellulose tripalmitate, cellulose trisuccinate, and cellulose trioctanoate; cellulose diacylates having a D.S. of 2.2 to 2.6 such as cellulose disuccinate, cellulose dipalmitate, cellulose dioctanoate, cellulose dipentate; coesters of cellulose such as cellulose acetate butyrate and cellulose, cellulose acetate propionate, and the like.

Please amend paragraph number **[0046]** as follows:

[0046] The osmotic pump 20 also includes the movable piston 30 (shown in FIGS. 2 and 3). The piston 30 is a member that is matingly received by the hollow interior of the capsule 22 and moves when subjected to pressure from the osmotic agent 26 to displace or move the beneficial agent 24. The piston 30 forms a ~~moveable~~ movable seal with the interior surface of the capsule 22. The ~~moveable~~ movable seal formed by the piston 30 separates the osmotic agent 26 and the beneficial agent 24 such that the osmotic agent does not substantially leak or seep past the piston seal and adversely affect the function of the beneficial agent. Hence, the osmotic agent 26 is separated from the beneficial agent 24 by the ~~moveable~~ movable piston 30.

Please amend paragraph number **[0048]** as follows:

[0048] The piston body 32 includes annular ring-shaped protrusions or ribs 38 that define the ~~moveable~~ movable or sliding seal with the inner surface of the capsule 22. The ribs 38 are the most outwardly radial surface of the piston body 32. The ribs 38 are the means by which the piston 30 forms a seal with the interior surface of the capsule 22. Thus, the outermost radial diameter 39 of the piston body 32 illustrated in FIGS. 2 and 3 includes four ~~ribs,~~ ribs; other ~~pistons~~ pistons, according to the present ~~invention~~ invention, may include one, two, three, or more ribs. Additionally, the piston body ~~32,~~ 32 need not include ribs. For example, the exterior surface of the piston body can be entirely cylindrical such that the entire cylindrical

exterior surface of the piston body affects a seal with the interior surface of the capsule 22. However, ~~the ribs~~ ribs 38 are preferred as they effect a better ~~moveable~~ movable seal with the interior surface of the capsule 22, as compared to a piston body having an exterior surface that is entirely cylindrical.

Please amend paragraph number **[0049]** as follows:

[0049] The number and size of ribs 38 on the piston body 32 ~~and their size~~ are determined by the amount of friction and the redundancy of seals desired in the piston 30. A cylindrical piston without ribs would increase the amount of friction between the piston 30 and the interior surface of the capsule 22. A large amount of friction between the piston 30 and the interior surface of the capsule 22 could lead to increases in start-up delay in order for the piston to overcome the friction with the interior surface of the capsule. The friction between the piston 30 and the interior surface of the capsule 22 could also lead to pulsatile delivery of beneficial agent 24 from the device or to a ~~stick/slip~~ slip-stick type of movement of the piston 30. If zero-order release of beneficial agent 24 is desired, then pulsatile or ~~slip-stick~~ slip-stick movement of the piston is unacceptable. The number of ribs 38 included on the piston body 32 is selected to provide a suitable seal between the osmotic agent 26 and the beneficial agent 24 during storage and operation of the osmotic pump 20, while maintaining the magnitude of friction generated between the piston 32 and the interior surface of the capsule 22 at a level that allows delivery of the beneficial agent 24 at a desired rate or rate profile.

Please amend paragraph number **[0050]** as follows:

[0050] The size and shape of the ribs 38 on the piston body 32 also play a role in the way the piston 30 moves in the capsule 22, and the amount of sealing provided by the piston 30. As the diameter 39 of the piston core 60 is increased, the depth of valleys 40 or areas between the ribs 38 decrease. As the valleys 40 are truncated, the space available for air to be entrapped during the process of inserting the piston 30 into the capsule 22 is reduced. Because air is

compressible, air in the capsule 22 must be compressed before the beneficial agent 24 can begin to be delivered from the capsule 22. Therefore, the ~~less the~~ less air that is entrapped between the ribs 38 of the piston body 32, the shorter the start-up time.

Please amend paragraph number **[0051]** as follows:

[0051] Truncation of the valleys 40 between the ribs 38 of a piston 30 of the present invention also works to reduce the springiness and the linear compressibility of the piston 30. A reduction in the compressibility reduces the start-up time for delivery of beneficial agent 24.

Please amend paragraph number **[0052]** as follows:

[0052] Where it is desired to provide an osmotic pump 20 with a coated piston 30, truncation of the valleys 40 between the ribs 38 of the piston body 32 also makes the piston 30 easier to coat. Coating of the piston 30 may include, but is not limited ~~to~~ to, coating done by known ~~liquid immersion and spray coating~~ liquid-immersion and spray-coating processes. As the depth of the valleys 40 formed between ribs 38 included on a piston 30 increases, the likelihood of an incomplete or ~~non-uniform~~ non-uniform coating also increases. In particular, as the depth of the valleys 40 formed between ribs 38 increases, the likelihood that the sides and bottom of the valley 40 will not be coated due to shadowing or obstruction by adjacent ribs 38 also increases. In addition, as the depth of the valleys 40 formed between the ribs 38 increases, the likelihood that a bubble of air will become entrapped therein during a coating process also increases. Therefore, truncation of the valleys 40 formed between ribs 38 included on a piston 30 of the present invention eases the task of providing the piston 30 with a uniform coating, where desired.

Please amend paragraph number **[0053]** as follows:

[0053] The piston 30 in the present invention is designed to maximize the beneficial agent 24 and/or osmotic agent 26 payload. This means that the piston 30 of the present invention

was reduced in size to allow for more beneficial agent 24 and/or osmotic agent 26 capacity without increasing the size of the capsule 22. The piston 30 of the present invention is reduced in size, exhibiting a ~~length to total width~~ length-to-total-width ratio of about 1.1:1 without any increases in leakage past the piston 30 or change in zero-order delivery of the beneficial agent 24. Moreover, to reduce the possibility of air entrapment around the ribs 38 of the piston body 32, the ribs 38 of the piston body 32 of the present invention are also reduced in size. In particular, the piston 30 of the present invention has a ~~core diameter to total diameter~~ core-diameter-to-total-diameter ratio of about 0.9:1.

Please amend paragraph number **[0054]** as follows:

[0054] In one embodiment of the present invention, the piston 30 has a length of 6.00 millimeters (0.237 inches) and a total diameter of 5.50 millimeters (0.217 inches), giving a ~~length to total diameter~~ length-to-total-diameter ratio of 1.1:1. The piston 30 in this embodiment also has a core diameter 39 of 4.90 millimeters (0.193 inches), giving a ~~core diameter to total diameter~~ core-diameter-to-total-diameter ratio of 0.89:1.

Please amend paragraph number **[0057]** as follows:

[0057] It is preferable that the piston body 32 be substantially impervious to liquids, such that the osmotic agent 26 and the liquid that permeates through the semipermeable body 28 does not diffuse through the piston body 32 and affect the beneficial agent 24 located on the side of the piston 30 opposite from that of the osmotic agent 26, and such that the beneficial agent 24 does not diffuse through the piston body 32 and affect the performance of the osmotic agent 26.

Please amend paragraph number **[0058]** as follows:

[0058] While the invention has been described in detail with reference to a preferred embodiment thereof, it will be apparent to one skilled in the art that various changes can be ~~made,~~ made and equivalents employed without departing from the spirit and scope of the invention.